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10/585,864	07/11/2006	Patrick Dawson Bailey	BJS-620-527	7738

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EXAMINER	
NIEBAUER, RONALD T	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,864	BAILEY, PATRICK DAWSON	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,6,10,12-24,28,29,31,32 and 40-46* is/are pending in the application.

4a) Of the above claim(s) *6,10,12-18,22,29,40 and 41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,19-21,23,24,28,31,32 and 42-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

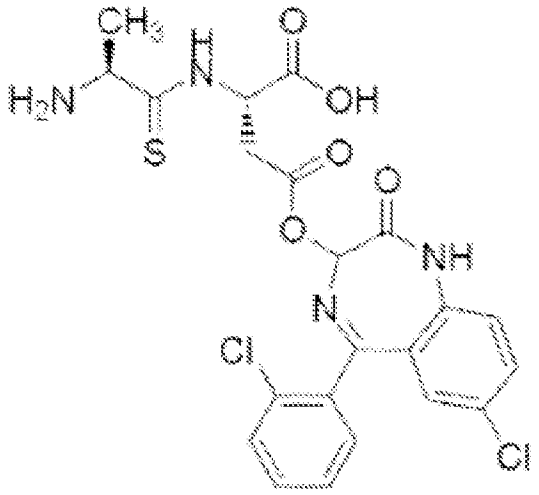
Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/25/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendments and arguments filed 3/24/10 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn. The previous 112 2nd rejections and the 102 rejections based on Wilner et al are withdrawn based on the amendments.

Previously, Applicant's elected Group 2 in the reply filed on 11/5/08 and the species of conjugate of:



in the reply filed on 7/20/09. The elected species was not found in the prior art. It is noted that no claim reads solely on the elected species. As such, whether or not the species is supported by the original specification has not been considered. In accord with section 803.02 of the MPEP the search was extended to another species. As discussed below, art was found that reads on the instant Markush-type claim as amended. As such, the examination has been extended to the

extent necessary to determine patentability of the Markush type claim but has not been extended unnecessarily to cover all nonelected species.

Claims 6,10,12-18,22,29,40-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/20/09.

Claims 1-2,4-5,7-9,11,25-27,30,33-39 have been cancelled.

Claims 3,19-21,23-24,28,31-32,42-46 are under consideration.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 3/25/10 has been considered by the examiner.

Claim Rejections - 35 USC § 112

Claims were previously rejected under 112 1st written description. Since the claims have been amended the rejection is updated.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3,19-21,23-24,28,31-32,42-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus …") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a

generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

Further, to provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include: a) the scope of the invention; b) actual reduction to practice; c) disclosure of drawings or structural chemical formulas; d) relevant identifying characteristics including complete structure, partial structure, physical and/or chemical properties, and structure/function

correlation; e) method of making the claimed compounds; f) level of skill and knowledge in the art; and g) predictability in the art.

(1) Level of skill and knowledge in the art/predictability in the art:

The level of skill in the art is high. There is unpredictability in predicting functional effects of replacements. It is not within the skill of the art to predict any and all replacements that would result in compounds that are capable of being released as recited in claim 31 or that are adapted to be transported by a PepT1 protein or a PepT2 protein as recited in claim 3

(2) Scope of the invention/Partial structure/disclosure of drawings:

In the instant case, the claims are drawn to drug conjugates. The specification broadly defines drug to include an active compound or molecule (page 2 lines 24-25). Further, it is noted that thiopeptide has been broadly defined (page 6 lines 1-4) such that a 'thio functional' group be present and such that (page 5 line 30) a peptide bond is not required. Claim 45 recites no formula. Claims 28 and 46 recite a formula but the claims are broad with respect to the R1,R4 and drug.

It is noted that figures 1 and 6 provide examples of conjugates. However, such conjugates are not representative of the scope of the instant claims. There is substantial variability in the genus. Since there are a substantial variety of compounds possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

(3) Physical and/or chemical properties and (4) Functional characteristics:

Claim 31 states that the compound is capable of being released. Claim 3 states that he compound is adapted to be transported by a PepT1 protein or a PepT2 protein. Further claim 28 refers to a 'drug conjugate' wherein the drug can be an active molecule. However, there is no specific disclosed correlation between structure and function. It is unclear what structural elements are required for the recited function. There are no common attributes or characteristics that identify compounds to be transported by a PepT1 or PepT2 protein. As such, one of skill in the art would not recognize a core structure, common attributes, or features of such compounds. One of skill in the art would not recognize drug conjugates outside of those specifically identified such as those in the Figures. There is no teaching in the specification regarding what part of the structure can be varied while retaining the ability to act as a drug or active molecule. In particular, no common core sequence is taught. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus and that there is a lack of the knowledge in the art regarding which amino acids can vary to maintain the function and thus that the applicant was not in possession of the claimed genus.

(5) Method of making the claimed invention/actual reduction to practice:

The specification (specifically page 25) describes the making of conjugate compounds. Figures 1,6 shows specific conjugates. However, such conjugates are not representative of the instant genus nor do the conjugates provide a specific correlation between structure and function

such that one could identify any and all drug conjugates where the compound is adapted to be transported by a PepT1 protein or a PepT2 protein.

As stated supra, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 3,19-21,23-24,28,31-32,42-46 is/are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are many. Although the claims may recite some functional characteristics, the claims lack written description because there is no specific disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of compounds identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Response to Arguments – 112 written description

Applicants argue (pages 12-15) that the examples describe representative species and that the R1 and R4 groups are described.

Applicants argue that the claims define a core structure.

Applicants argue that figures 1 and 6 show conjugates.

Applicant's arguments filed 3/24/10 have been fully considered but they are not persuasive.

Although Applicants argue (pages 12-15) that the examples describe representative species and that the R1 and R4 groups are described, it is first noted that claim 45 does not include an R1 or R4 group. Further, the R1 and R4 groups are broad. It is also noted that the claims are to drug conjugates. A description of the R1 group is not sufficient to describe the drug. With regards to examples, applicants expressly admit (page 14 lines 24-26) that the molecules did not have biological activity.

Although Applicants argue that the claims define a core structure, it is first noted that claim 45 includes no structure. Further, the formulas shown do not define the drug of the drug conjugate. Further the side chain groups R1, and R4 are broad. The defining features of a peptide are the side chain groups and one would not recognize the backbone of the peptide as a significant core structure.

Although Applicants argue that figures 1 and 6 show conjugates, Applicants expressly admit (page 14 lines 24-26) that the molecules did not have biological activity. Absent a structre/function relationship one would not recognize the features required for transportation by PepT1 (see claim 3), or the capability of being released (see claim 31).

Claim Rejections - 35 USC § 102

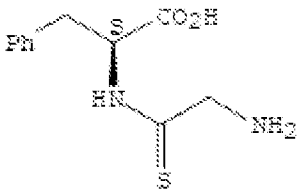
This 102 rejection is necessitated by applicants amendments.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3,19-21,23-24,28,31-32,42-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Mcelroy et al ('Gly-(CSNH)-Phe resists hydrolysis by membrane dipeptidase' Biochemical Society Transactions (1998) 26(1) S31).

Mcelroy teach the peptide Gly-(CSNH)-Phe of structure



Mcelroy teach that the peptides were purified by RP-HPLC and measurements confirmed their identity and that the peptides were used in a buffer in experiments (paragraphs 2-3). In relation to the instant claims, R1 is hydrogen thus meeting the limitations as recited in claims 23-24,28,46 of the instant claims. R4 comprises an alkyl attached to a functional group and comprises CH2 thus meeting the limitations as recited in claims 19-21,28,45,46. Mcelroy teach both the R (i.e.

D) and S (i.e. L) forms and specifically teach Gly-(CSNH)-Phe of the structure shown above thus meeting the limitations as recited in claims 42-44. The compound of Mcelroy has an N- and C-terminal residue and a carboxylic acid group as recited in claim 45. Mcelroy teach that the peptides were purified by RP-HPLC and measurements confirmed their identity and that the peptides were used in a buffer in experiments (paragraphs 2-3) thus the compounds were in a form of a medicament as recited in claim 32. It is noted that pages 2-3 of the specification defines drug as an active molecule and states that the drug may not be used in medicine. Further, the specification shows (Figure 1,6) examples of the drug groups. In the instant case, the Ph group as taught by Mcelroy is a group as shown in Figure 1b. Thus it is consistent with applicants specification that the claim limitations are met.

It is noted that claims 3,31 refer to properties. Since the compound of Mcelroy meet the structural limitations the functional limitations are met absence evidence to the contrary (see MPEP section 2112.01). It is noted that claim 46 recites 'being a product'. Section 2113 of the MPEP states: “[E]venthough product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” In the instant case, Mcelroy teach the product thus the claim limitations are met.

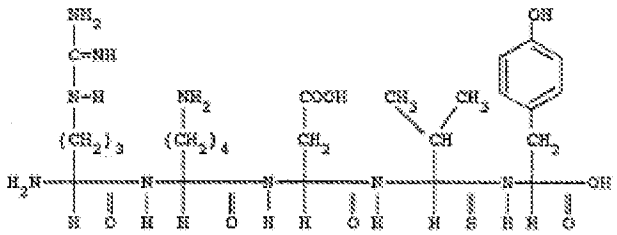
A rejection based on Brillon appeared in the previous office action. Since the claims have been amended an updated rejection appears herein.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 45 is rejected under 35 U.S.C. 102(b) as being anticipated by Brillon et al (WO 91/01976 as cited in IDS 11/27/06).

Brillon teach using thioamide bonds in peptides (abstract). Brillon teach that the incorporation of thioamide linkages increases resistance to enzymatic digestion (page 23 lines 13-16). Brillon teach that 4-thiothymopentin (formula VII page 22, also example 4 page 45)



(VII)

has higher biological activity than the unmodified polypeptide.

In relation to claim 45, 4-thiothymopentin (formula VII page 22) is a thiopeptide (It is noted that the instant specification (page 6 lines 1-4) defines thiopeptide such that a 'thio functional' group be present and such that (page 5 line 30) a peptide bond is not required) which

comprises a C-terminal carboxylic acid, and an N-terminal residue. It is noted that the claims recite 'comprising' so the compound is not limited to being a dipeptide. It is noted that pages 2-3 of the specification defines drug as an active molecule and states that the drug may not be used in medicine. Further, the specification shows (Figure 1,6) examples of the drug groups. In the instant case, the Ph-OH group as taught by Brillon is a group consistent with those shown in Figure 1b/c. Thus it is consistent with applicants specification that the claim limitations are met.

Response to Arguments – 102 Brillon

Applicants argue (page 15) that Brillon does not disclose the formula recited in the pending claims.

Applicant's arguments filed 3/24/10 have been fully considered but they are not persuasive.

Although Applicants argue (page 15) that Brillon does not disclose the formula recited in the pending claims, claim 45 does not recite a formula. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., formula) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Related Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Hubbell et al (US 20030220245, cited previously). Hubbell teach (page 40 example 12, especially section 0406) thiol peptide drug conjugates.

Conclusion

In the instant case, applicants have amended the claims. Applicants amendments have necessitated any new grounds of rejection.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654

/Ronald T Niebauer/
Examiner, Art Unit 1654